tivities as high as 92% to 100% have been found. The comparison studies are especially convincing because the same patient's leukocytes can be labeled with both ^{111}In-tropolone and [^{99m}Tc]HMPAO and then imaged simultaneously using different energy windows.

The most exciting advantage of [^{99m}Tc]HMPAO-labeled leukocytes over other labels is their ability to detect sites of infection within 30 minutes of administration. Leukocytes labeled with indium In 111 oxyquinolone detect as few as a third of cases of infections when imaged in the first 4 hours after administration; 24-hour delays are common (although some studies with ^{111}In-oxine- and ^{111}In-tropolone-labeled cells have shown a high sensitivity for infection in the first few hours after injection). The much more rapid diagnosis with [^{99m}Tc]HMPAO allows antibiotic or surgical therapy to be instituted earlier.

Leukocytes labeled with [^{99m}Tc]HMPAO have a number of other advantages as well. Unlike ^{111}In-oxine, HMPAO labeling can be done in plasma, which enhances cell viability and prevents leukocyte activation. Technetium HMPAO is a more specific granulocyte label than ^{111}In-oxine; in addition, the tag is eluted primarily from monocytes, resulting in a nearly pure granulocyte label without the need to do complicated separation techniques such as density gradient centrifugation.

Compounds containing ^{99m}Tc provide better images than those containing ^{111}In or gallium 67 because its energy is ideal for today's gamma cameras. The radiation exposure to the patient is reduced by a third to a half compared with ^{111}In-labeled cells. Technetium is always available because it is obtained from generators on site rather than being shipped in. Finally, ^{99m}Tc is considerably less expensive than the other commonly used radioisotopes.

There are some problems with [^{99m}Tc]HMPAO-labeled leukocytes, however. Bowel, biliary, and genitourinary excretion occurs. Because bowel activity does not appear until four hours after administration, early imaging will usually prevent false-positive diagnoses. Indium 111–labeled leukocytes, however, are not normally excreted into the bowel and therefore have an advantage in imaging abdominal and pelvic infections. Also, chronic infections in which leukocyte exchange is slowed may not be seen as well with [^{99m}Tc]HMPAO-leukocytes, as delays of 4 to 24 hours between administration and imaging may be required. Lower uptakes of [^{99m}Tc]HMPAO-granulocytes compared with ^{111}In-labeled leukocytes are seen in experimentally induced abscesses at 18 hours after administration due to elution of the [^{99m}Tc]HMPAO label with time. Finally, [^{99m}Tc]HMPAO labeling of leukocytes for infection imaging is not currently approved by the US Food and Drug Administration and therefore may not be available at all sites.

In summary, [^{99m}Tc]HMPAO-leukocytes are an important new technique for imaging acute infection. For more chronic infections, in suspected infection of organ systems that normally excrete [^{99m}Tc]HMPAO, or in cases where a rapid answer is not needed, ^{111}In-leukocytes or ^{67}Ga-gallium citrate may be better choices.

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Radionuclide Evaluation of Brain Death

SUCCESSFUL TRANSPLANTATION OF cadaveric organs requires the removal of organs soon after the donor's death. A prompt determination of the donor's death is necessary to avoid deterioration of the organs to be transplanted. How can it be determined when or if a critically injured, deeply comatose person on life support has died?

Since a landmark publication in 1968 by the Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death, there have been several revisions of the criteria. The currently most widely accepted criteria were established in a report to the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. These "Guidelines for the Determination of Death" state that a person with irreversible cessation of circulatory and respiratory function is dead and that a person with irreversible cessation of all functions of the entire brain, including the brain stem, is dead.

In the case of a comatose person who is mechanically ventilated, the first criterion does not apply. When the patient is determined to be neurologically dead, death can be confirmed by showing absent brain blood flow. Absent blood flow to the brain is incompatible with life. As brain tissue dies, it swells. Intracranial pressure increases, resulting in a progressive reduction of circulation to the brain. When the intracranial pressure reaches systolic pressure, circulation ceases.

A lack of brain blood flow is well shown by four-vessel contrast angiography, which is accepted as legal proof of brain death in Germany and the Scandinavian countries. Alternative methods of brain death confirmation include digital subtraction angiography and dynamic computed tomography. All of these methods require transport of the person to the imaging area.

Radionuclide cerebral angiography using diethylenetriaminepentaacetic acid (DTPA) labeled with technetium 99m has been shown to be as accurate as contrast angiography in confirming brain death. The method is noninvasive and relatively inexpensive, and, most important, it can be done at the bedside using a portable gamma camera and computer. It is quick and easy to do. Radionuclide cerebral angiography has two disadvantages. A good intravenous bolus is essential. A poor bolus or equipment malfunction during the flow study may make the study uninterpretable, in which case it would need to be repeated. Also, radionuclide cerebral angiography demonstrates the presence or absence of cerebral blood flow and does not evaluate blood flow to the cerebellum, midbrain, or medulla. Therefore, it does not meet the strict criterion of the total absence of brain blood flow.

Technetium 99m-hexamethyl propyleneamine oxime (HMPAO) is a new lipophilic agent used for cerebral perfusion imaging. It is taken up by grey and white matter in proportion to blood flow (4:1). Normally the cerebellum is visualized. Therefore, the agent can answer the question, Is there subtentorial blood flow? Imaging is not dependent on a good intravenous bolus and is not subject to fluctuations in a hospital's electrical supply. If an image is lost because of, for example, an electrical surge, it can be repeated immediately with no significant delay. Disadvantages are the relatively high cost of an HMPAO kit and its instability after preparation: The tracer should be injected within 30 minutes of

preparation. Excellent correlation with radionuclide cerebral angiography has been shown. This is likely to become the technique of choice for confirming brain death.

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Radionuclide Therapy for Thyroid Disease

ONE OF THE GOALS OF therapy is to deliver the active agent directly to the disease site and to have the rest of the body subjected to as little of the agent as possible. This principle is even more important when therapy with systemic radionuclides is considered. Iodine therapy for thyroid diseases meets this goal.

Radioiodine has a role as a primary treatment of hyperthyroidism. It also has a role in the treatment of differentiated papillary and follicular thyroid cancer. Of the hyperthyroid states, the most common is Graves' hyperthyroidism. This is ideally treated with radioiodine because the gland is diffusely involved and the uptake of radioiodine is usually greater than 50% of an administered dose. Patients of all ages can be treated. Contraindications to treatment are pregnancy and breast feeding.

Although over the years there has been debate about the appropriate therapeutic dose, some investigators try to select a dose that would bring the patient to a euthyroid state. Long-term experience, however, has dictated that this goal is often not achievable. I now advise prescribing one therapeutic dose designed to cure hyperthyroidism with the expectation that permanent hypothyroidism will occur. The patient should be counseled and recognize the need for life-long thyroid hormone replacement.

Single toxic nodules and toxic multinodular goiters can also be treated with radioiodine therapy. These conditions, in general, are somewhat more resistant to irradiation, and the prescribed dose is proportionately greater. In contrast to Graves' disease where the thyroid becomes impalpable after the administration of sodium iodide I 131, nodular goiters treated with radioiodine often are still palpable and the patient is rendered euthyroid. The incidence of posttreatment hypothyroidism is lower after the treatment of nodular goiters with ^{131}I-sodium iodide. Long-term follow-up has failed to show an increased risk of cancer or genetic abnormalities in the offspring of patients treated with ^{131}I-sodium iodide.

Radioiodine therapy for thyroid cancer is an adjuvant treatment that is given in selected patients after the primary lesion has been removed surgically. It is frequently used to ablate remnants of presumed normal thyroid after the operation. The exact role of this is still open to debate. It can also be used to treat functioning metastases in regional lymph nodes and in distant organs such as the lungs or bones. A preparatory whole-body scintiscan using ^{131}I shows the extent of disease. Should this treatment be considered, it is extremely important to discontinue exogenous thyroxine therapy and to demonstrate that the thyrotropin level is elevated. It is also important to ensure that large doses of exogenous iodine, in particular, radiographic contrast, are not given for

several weeks before radioiodine therapy. If a dose of 30 mCi or more is prescribed, the patient should be admitted to hospital until the retained dose falls below that level. This treatment is well tolerated compared with systemic chemotherapy and external beam therapy. The long-term hazards that might be anticipated, including the occurrence of second malignant neoplasms, have not been described in several large follow-up studies.

Serious complications of radioiodine therapy such as thyroid storm and acute thyroiditis are extremely uncommon. Data published recently do not support a relationship between the occurrence of infiltrative ophthalmopathy and treatment with radioiodine.

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Diagnostic and Therapeutic Uses of Metaiodobenzylguanidine

METAIODOBENZYLGUANIDINE (MIBG), a guanethidine analogue developed as an adrenal imaging agent, shares a specific uptake and storage mechanism with norepinephrine. Since its introduction as a radiopharmaceutical, numerous studies have documented its high sensitivity (90%) and specificity (100%) for detecting pheochromocytoma and neuroblastoma. Consequently, MIBG has gained prominence not only in the diagnosis but also in the staging and posttherapeutic evaluation of these tumors. This agent also localizes in carcinoid (40%) and various other neuroendocrine tumors, but with less sensitivity.

When radiolabeled with either iodine 123 or iodine 131, MIBG normally localizes in the salivary glands, heart, liver, and urinary bladder with occasional uptake in lacrimal glands, normal adrenal glands, and colon. Because bone uptake is not expected in the absence of tumor involvement, osseous metastases can be easily identified.

There are several instances in which the normal biodistribution of MIBG is altered. The use of interfering medications such as tricyclic antidepressants, phenothiazine, labetalol, decongestants, and cocaine may result in a nondiagnostic or falsely negative study. These medications should be discontinued at least seven days before obtaining an MIBG scan.

Metaiodobenzylguanidine scans are indicated in several conditions. If a mass is present, an MIBG scan can indicate whether it is of neuroectodermal origin. This can be useful in hypertensive adults with incidentally discovered adrenal masses on computed tomography scans. Also, because 10% to 30% of pheochromocytomas are multiple, or extra-adrenal, these can be detected, ensuring a good surgical result. Finally, because of the occasional histologic confusion over "small blue cell" neoplasms in children, MIBG scanning can be crucial in making a diagnosis of neuroblastoma.

Compounds comprising MIBG labeled with ^{131}I and, more recently, ^{125}I are under investigation as parenteral radiotherapeutic agents to be used in advanced cases of both pheochromocytoma and neuroblastoma. Initial results